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(71) Applicants *(for all designated States except US)*: **YISSUM RESEARCH DEVELOPMENT COMPANY OF THE HEBREW UNIVERSITY OF JERUSALEM** [IL/IL]; Hi Tech Park, Edmond Safra Campus, Givat Ram P.O. Box 39135, Jerusalem 39135 (IL). **BEN-GURION UNIVERSITY OF THE NEGEV RESEARCH & DEVELOPMENT AUTHORITY** [IL/IL]; P.o. Box 653, 84105 Beersheva (IL). **MOR RESEARCH APPLICATIONS LTD.** [IL/IL]; 23 Hasivim Street, Kiryat Matalon P.O.Box 7590, 49170 Petach Tikva (IL).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **SOREQ, Hermona** [IL/IL]; 14 HaMaayan Street, 95930 Jerusalem (IL). **BEN-MOYAL, Liat** [IL/IL]; 11 Barkan Street, 84965 Omer (IL). **BRYK, Boris** [IL/IL]; 33/209 Rabinovitz Street, 96549 Jerusalem (IL). **FRIEDMAN, Alon** [IL/IL]; 5 Binyamin Street, 70700 Gedera (IL).

(74) Agents: **LUZZATO, Kfir** et al.; Luzzato & Luzzato, P.O. Box 5352, 84 152 BeerSheva (IL).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PARKINSON'S DISEASE SUSCEPTIBILITY HAPLOTYPE AS A TOOL FOR GENETIC SCREENING

(57) Abstract: Specific PON1 and ACHE alleles segregate in linkage, forming an haplotype which directly correlates with higher susceptibility to develop Parkinson's Disease (PD). This PD-susceptibility haplotype is herein presented as a tool for predicting the risk of developing Parkinson's Disease and its severity, both for an individual and for the population in general. Thus, the present invention provides the use of said PD-susceptibility haplotype in diagnostic and screening methods.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL 03/00764

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BIOSIS, MEDLINE, EPO-Internal, WPI Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	AKHMEDOVA SOFYA N ET AL: "Paraoxonase 1 Met-Leu 54 polymorphism is associated with Parkinson's disease" JOURNAL OF THE NEUROLOGICAL SCIENCES, vol. 184, no. 2, 1 March 2001 (2001-03-01), pages 179-182, XP002267680 ISSN: 0022-510X abstract --- -/--	1-4

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 January 2004	04/06/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bradbrook, D

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL 03/00764

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SHAPIRA MICHAEL ET AL: "A transcription-activating polymorphism in the ACHE promoter associated with acute sensitivity to anti-acetylcholinesterases" HUMAN MOLECULAR GENETICS, vol. 9, no. 9, 22 May 2000 (2000-05-22), pages 1273-1281, XP002906056 ISSN: 0964-6906 abstract	1-4
A	KONDO IKUKO ET AL: "Genetic polymorphism of paraoxonase 1 (PON1) and susceptibility to Parkinson's disease" BRAIN RESEARCH, vol. 806, no. 2, 28 September 1998 (1998-09-28), pages 271-273, XP001031094 ISSN: 0006-8993 abstract	1-4
A	BARTELS CYNTHIA F ET AL: "Mutation at codon 322 in the human acetylcholinesterase (ACHE) gene accounts for YT blood group polymorphism" AMERICAN JOURNAL OF HUMAN GENETICS, vol. 52, no. 5, 1993, pages 928-936, XP009023769 ISSN: 0002-9297 the whole document	1-4
A	CARMINE ANDREA ET AL: "Further evidence for an association of the paraoxonase 1 (PON1) Met-54 allele with Parkinson's disease." MOVEMENT DISORDERS: OFFICIAL JOURNAL OF THE MOVEMENT DISORDER SOCIETY. UNITED STATES JUL 2002, vol. 17, no. 4, July 2002 (2002-07), pages 764-766, XP009024201 ISSN: 0885-3185 abstract	1-4
A	KAUFER D ET AL: "Tracking cholinergic pathways from psychological and chemical stressors to variable neurodeterioration paradigms." CURRENT OPINION IN NEUROLOGY. ENGLAND DEC 1999, vol. 12, no. 6, December 1999 (1999-12), pages 739-743, XP009024183 ISSN: 1350-7540 page 740, column 2, paragraphs 3,4	1-4

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-4 (in part), 5 (in full)

The feature "Parkinson's Disease (PD)-susceptibility haplotype", referred to in claims 1-5, is unclear and therefore renders said claims unclear (Art.6 PCT). Furthermore, the feature "as herein defined", used in claims 1-3, is vague and does not render the meaning of the claims clear from the wording of the claims alone. The search has been carried out on the basis of said haplotype being that defined on p.19, last 3 lines, i.e. comprising the PON1 alleles L55M and Q192R, and ACHE alleles delHNF3, H332N and P446.

Claim 5 is directed to a kit comprising means for collecting a blood sample and reagents for detecting the PD-susceptibilty haplotype. Said reagents are not further defined, so that the content of the kit is unclear (Art.6 PCT). Whilst the description makes reference to methods for the detection of polymorphisms (cf pages 20-23), there is no indication as to any specific reagents which may be packaged together in kit form. Therefore, no search has been carried out for said claim 5.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL 03/00764

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-4 (in part), 5 (in full)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.